Section of Surgery

President A S Till MChir

Meeting November 4 1964

President's Address

Carcinoma of the Thyroid

by A S Till MChir
(Radcliffe Infirmary, Oxford)

There are four main problems which make thyroid carcinoma a remarkable disease: (1) Its very varying natural history, being virtually two diseases. (2) The unusual difficulties of histological interpretation. (3) The nature of its ætiology. (4) The question of hormone dependency. On all these depend the proper scope of surgery in prophylaxis and treatment and the appropriate use of radioactive isotopes.

In a rare disease the experience of any one surgeon is of necessity rather limited and my own is no exception. In Oxford, during the years 1952–62, I have studied 205 cases registered in the Regional Hospital Board area, 44 of whom have been under my own personal care and it is on these that my Address is based.

History

To surgeons of the past the problem seemed perhaps less complex than it does today for, though they were well aware of endemic goitre, there was little that could be done for its sufferers except the empirical use of iodine and occasionally the seton. Such an obvious condition could hardly escape notice; the medical literature of the last three centuries records the disease, the areas in which it was commonly found and the many theories put forward for its causation. The possibility of malignant change in the more usual type of endemic goitre had not gone unnoticed and was well recognized in early times. Heister (1748), when writing of bronchocele – the old term for goitre, refers not only to cretinism associated with goitre but also to goitres 'of a malignant or cancerous disposition so as to be schirrous and in some measure obstructing the orifice of respiration and deglutition'. The first English book devoted solely to goitre, entitled 'The English Bronchocele', was written by Inglis in 1838, in which the author describes cases of the tumour becoming cancerous and destroying the patients. It seems clear that endemic goitre in those days in England was much commoner and more florid than at present and, according to Inglis, especially so in Yorkshire, Derbyshire, Hampshire, Sussex and Surrey. In his view, the condition was hereditary, and on occasion associated with cretinism for he stated that the 'intermarrying and otherwise of these wretched beings repopulated a district with a progeny more disgusting than themselves'. There are few references to goitre in the classical writings of the great English surgeons in the eighteenth and nineteenth centuries until the time of Paget, though King & Astley Cooper (1836) described in great detail the anatomy of the thyroid gland and its lymphatic drainage, a knowledge of which is of value today in deciding on the proper operative procedures for the treatment of carcinoma. As one might expect, Billroth had considerable knowledge of goitre and in 1878 described the development of cancerous bronchoceles with involvement of adjacent lymphatic glands. Sir James Berry (1901) and Sir John Bland-Sutton (1901) both described in considerable detail much of what we know today about the natural history of this disease: we cannot read the works of either without humility, wondering whether we really are more successful in treatment than they were. Bland-Sutton recorded only three personal cases of thyroid cancer in twenty years' practice but he was well aware of the possibility of tumours in young girls, and of pulsating bony metastases. Likewise, Berry appreciated the very different natural history of the 'papilliferous cystic carcinoma', as he called it, as distinct from what was termed 'sarcoma'.

Incidence and Ætiology

Thyroid carcinoma today accounts for about 350 deaths a year in England and Wales, less than 1% of all cancer. Although rare, it is not more so proportionately nowadays than carcinoma of the tongue, of the testicle or of bone and joint sarcoma. Compared with benign lesions of the thyroid, where women predominate by 10 to 1,

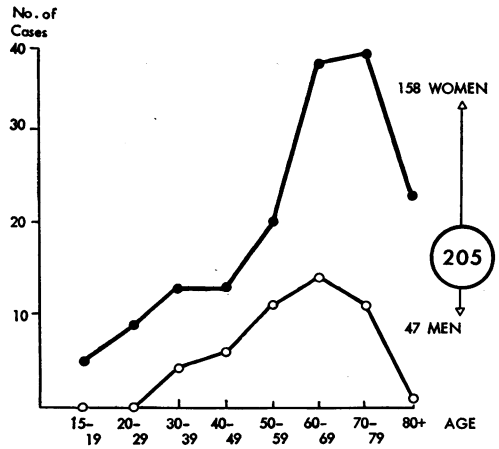

Fig 1 *Age and sex distribution of 205 cases of carcinoma of the thyroid seen between 1952 and 1962*

the reason for which is obscure, in cancer of the thyroid the sex ratio is only 3 women to 1 man – a fact which must be significant when considering the nature of goitres in men (Fig 1). A higher proportion of tumours occur in the under 40s than is usually the case with carcinoma in other sites.

Mortality statistics take no account of the many thyroid cancers which occur and which are successfully treated: a better index of the incidence of the disease is afforded from those cases registered by the Regional Cancer Records Bureaux (Fig 2); their returns show that between 10 and 16 new cases per million population are recorded every year in the United Kingdom. It was originally thought that thyroid cancer was more common in endemic areas, such as Berne in Switzerland, but the evidence supporting this view has become far less convincing and in 1953 the World Health Organization was unable to express an opinion on this important point. Fig 2 shows that thyroid cancer is fairly evenly distributed throughout this country and that the higher incidence which one might have expected in the so-called goitrous areas does not in fact exist. Indeed the incidence is higher in some non-goitrous areas.

Goitrous areas were previously defined from the examination of school children but there is no evidence that enlargement in childhood necessarily runs parallel with endemic goitre in adults. It is more probable that in this country, with improved hygiene, better food, water containing adequate supplies of iodine and a shifting population, the regional distribution of goitre may well have been smoothed out. Essential as it is for prevention of goitre, there is no evidence that iodine prophylaxis will reduce the incidence of thyroid carcinoma.

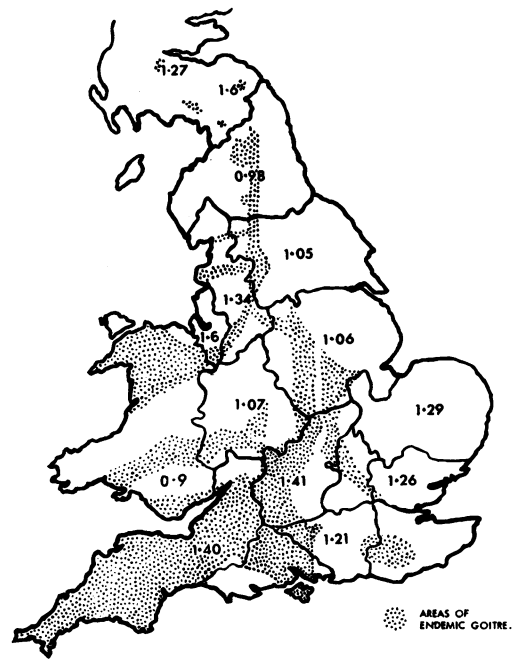

Fig 2 *Crude incidence rate of carcinoma of thyroid per 100,000 population per annum, by hospital region, during the years 1952–62. Areas of endemic goitre are stippled*

The vexed subject of malignant degeneration of simple nodular goitre can be approached in a more direct way by examination of operation material and by consideration of the duration of the goitre prior to a diagnosis of malignancy being made.

The comparison of statistics in this respect is, however, fraught with difficulties due to the methods of presentation, histological interpretation and many other factors. I will confine myself to our own findings in operation specimens from thyroidectomy – admittedly a highly selected group; the overall percentage showing carcinoma is generally considered to be of the order of 3% to 6% (Table 1): in my own series of 1,114 thyroid

Table 1
Thyroidectomy 1947–64

	No. of cases	%
Nontoxic nodular goitre	494	44·4
Diffuse toxic goitre	298	26·8
Nodular toxic goitre	219	19·7
Carcinoma	44	3·9
Recurrent goitre	25	2·2
Lymphadenoid	18	1·6
Diffuse nontoxic goitre	11	1·0
Riedel's thyroiditis	5	0·4
Total	1,114	100

Table 2
Solitary nodules of thyroid

	No. of cases
Nontoxic colloid	155
Cysts	26
Microfollicular adenomata	22
Carcinoma	12 (5·5%)
Total	215

operations 44 (3·9%) were malignant. Three cases were found in diffuse toxic goitres; the remaining 41 arose *de novo* or in nodular goitres. It is more important to get some idea of the incidence of occult carcinoma and I find that it is a good deal lower than has been reported elsewhere: if one excludes those cases which were manifestly malignant when first seen, only 14 cancers were found unexpectedly in 508 thyroidectomies for nontoxic nodular goitre. Twelve of these were discovered in solitary nodules – an incidence of 5·5% (Table 2); only 2 were found unexpectedly in the remaining 293 goitres with multiple nodules – less than 1%. The duration of goitre prior to the diagnosis of malignancy is not easy to determine – many patients being unaware of minor degrees of enlargement; however, of all the cases I have treated, about half have complained of a goitre for two years or less, and these were possibly malignant all the time, whilst only a quarter of the whole series developed a carcinoma in goitres of very long standing – twenty years' duration and more (Fig 3).

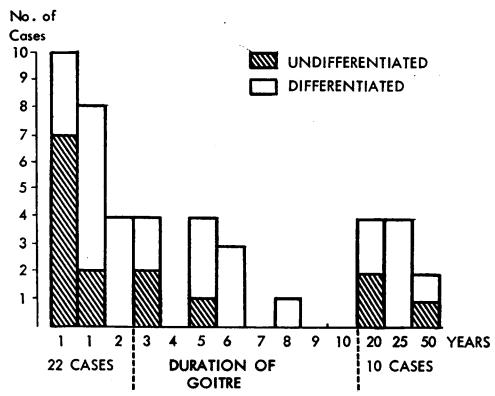

Fig 3 *Duration of goitre before diagnosis of carcinoma (44 cases)*

In summary, these figures agree with the well-known and accepted likelihood of malignancy in solitary nodules but suggest that occult carcinoma in multinodular goitres is probably rare. It appears that these multinodular glands probably do carry a slightly increased chance of malignant degeneration but that the risk is not great enough to advise routine thyroidectomy for all such goitres without other indications. Indeed a previous thyroidectomy has not always prevented a subsequent malignant change, since we have performed thyroidectomies for carcinoma in 2 patients whose goitres were removed many years previously.

Table 3
Carcinoma of thyroid, 1952–62 inclusive: number of cases registered Oxford Regional Hospital Board series

Year	*No. of cases*
1952	11
1953	14
1954	17
1955	14
1956	18
1957	14
1958	23
1959	19
1960	19
1961	28
1962	28
Total	205 (female 158, male 47; ratio 3 : 1)

One of these patients had been operated on at the age of 24 in the Middlesex Hospital by Sir Alfred Pearce Gould for a multiple cystic bronchocele. The multiple cysts were removed under ether anæsthesia and a cyanide dressing was applied. Post-operative bleeding was controlled by the application of sandbags, but a good recovery resulted and the patient was discharged home to Oxfordshire on the seventh post-operative day. Fifty-four years later he was admitted to the Radcliffe Infirmary with a recurrent goitre and a paralysed left vocal cord. A further thyroidectomy was carried out for a differentiated carcinoma. He survived two years, dying of a carcinoma of the prostate.

The incidence of thyroid carcinoma in the Oxford Region appears to have doubled in the last ten years (Table 3) but, even taking into account the increase in the population and possibly more accurate registration, I doubt if these figures imply any real increase in the disease. I suspect that we are now more alert to its possibilities and, by investigating patients with thyroid enlargement more accurately, we find and remove more malignant tumours; as an example of this we have discovered two papillary adenocarcinomata in patients who were being investigated and treated for other conditions, one with a carcinoma of the colon, the other with a duodenal ulcer, neither of whom had complained of any lump in the neck.

The relationship between ionizing radiation of the neck in infancy or childhood and the subsequent development of carcinoma is well known but fortunately no case in the present series could be attributed to this cause.

Pathology

The difficulties in the histological diagnosis of thyroid cancer and the possibility of the multifocal origin of the disease are, I am sure, best explained by consideration of the experimental production of thyroid cancer in animals. It has been conclusively shown that a prolonged increase in the output of thyrotrophic hormone by the pituitary, induced either by iodine deficiency, the administration of goitrogens such as thiouracil, partial thyroidectomy or by irradiation of the thyroid, will stimulate the thyroid and produce progressive changes – hyperplasia, benign adenomata and metastasizing carcinoma, which ultimately become anaplastic (Doniach 1956). These experiments emphasize the importance of the dynamic biological character of these tumours rather than their static cellular morphology; they explain perhaps why different histological types of tumour may overlap and change their character and how areas of carcinoma *in situ* may be found in several different parts of the gland.

We have thus got away from those classifications of thyroid tumours which were once so numerous and so complicated; they have gradually been reduced to a single one in which three types only are recognized – the papillary, the follicular and the anaplastic. Even this modification, though perhaps useful for practical purposes, is not quite as neat as might appear at first sight and for that reason the simplification has gone even further, so that only two types of tumour are recognized – the differentiated and the undifferentiated.

There seems little difficulty in pigeon-holing tumours at each end of the scale – the well-differentiated papillary ones, or the undifferentiated anaplastic. The middle group, commonly designated follicular, has rather wider variations of structure and has been diagnosed by our pathologists as adenocarcinoma – containing some which are purely adenomatous and those showing a more or less follicular pattern; being intermediate their behaviour will be more unpredictable and the treatment less definite. Our own series from the Oxford region has been histologically diagnosed and analysed along these lines (Table 4) and is comparable with other series published in this country: in the majority of series about two-thirds of the cases are differentiated and one-third undifferentiated.

A few atypical tumours are found from time to time. A small percentage may show areas of squamous metaplasia or be wholly squamous carcinomata – if this point is not appreciated the biopsy of involved lymph nodes may be misleading and result in an error of diagnosis, of which I have myself been guilty. These tumours carry a bad prognosis.

Table 4

Carcinoma of thyroid, 1952–62 inclusive: sex and type of histology
Oxford Regional Hospital Board series

	Male	*Female*	*Total*	*%*
Adenocarcinoma	19	62	81	39·5
Papillary	2	17	19	9·2
Anaplastic	11	30	41	20·0
Squamous	2	4	6	3·0
Unclassified	13	45	58	28·3
Total	47	158	205	100

Two other unusual types of thyroid tumour have occurred in the present series – these are the so-called struma reticulosa and struma ovarii. The first was a reticulosarcoma occurring in both thyroid and small bowel; the second was the malignant degeneration of thyroid tissue in a teratoma of the ovary with spread to the bony pelvis in a patient who survived for seven years after treatment with radio-iodine.

Diagnosis

The clinical diagnosis of anaplastic carcinoma is seldom difficult, and generally follows a textbook picture: arising in the elderly, most commonly in the seventh and eighth decades, in a previously normal or nodular thyroid, there is a rapid increase in the size of the gland which becomes hard, fixed and often painful; there may be dyspnœa and dysphagia (the latter being uncommon in benign goitre) with invasion of lymph nodes and metastases in lungs and occasionally bone; the recurrent and cervical sympathetic nerves may be paralysed. This picture has occurred in whole or in part in virtually all our anaplastic growths and it always surprises me to read of the lucky finding of an unexpected anaplastic tumour in excised nodular goitres. This type of the disease is particularly distressing, for its progress is obvious to all, including the patient who generally succumbs to slow strangulation in a matter of months despite treatment.

How different is the picture presented by the differentiated tumour which is by no means obviously malignant. In its simplest form it may present only as a nodule in the thyroid. One should be deterred neither by the length of history nor by the size of such symptomless solitary swellings; I have excised several papillary adenomatous carcinomas which were as large as an orange and had been present for several years.

No reliance can be placed on the consistency or mobility of a solitary nodule in making a diagnosis, though one which has come up very suddenly as a result of a hæmorrhage and progressively diminishes can probably be watched. The only safe course is to regard every recent enlargement of the thyroid with suspicion and

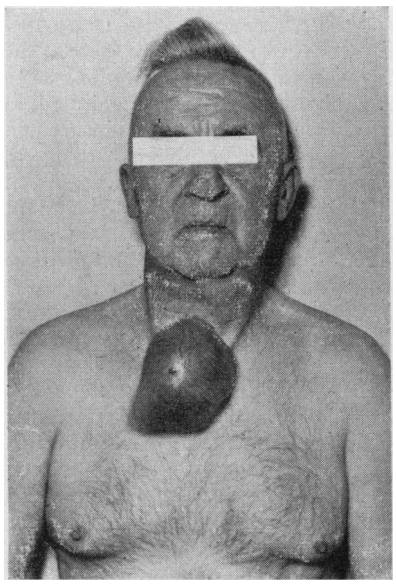

Fig 4 *Unusual extension of papillary adenocarcinoma*

every solitary nodule as malignant until proved otherwise.

Occasionally no lump at all can be felt in the thyroid, only the secondary nodes in the neck which are generally multiple, though only one may be easily palpable. These glands, too, may have been present for many years, so long that they may never have worried either the patient or her doctor. In two cases secondary nodes had been present for twenty and twenty-five years respectively.

Apart from lymphatic and vascular spread, occasionally carcinoma of the thyroid may infiltrate locally in an unusual way, as illustrated by Fig 4 which shows a patient whose growth had spread through the deep cervical fascia on to the chest wall.

Malignancy may be associated with thyrotoxicosis and has occurred in 3 cases of diffuse toxic goitre in my own series. One of these was an undoubted encapsulated Hürthle cell tumour, the other 2 being found in very hyperplastic glands, one of which had occurred with recurrent thyrotoxicosis. The differentiation of malignancy from thyrotoxic hyperplasia may, however, be most difficult.

Laboratory investigations are of little value in diagnosing thyroid carcinoma, though they are useful in a negative way by excluding other conditions such as thyrotoxicosis, thyroiditis and some reticuloses. Scanning of the neck after radio-iodine may be useful in recognizing 'hot' nodules which are very unlikely to be malignant and, therefore, do not require urgent excision. On the whole we prefer an open operation to a needle biopsy, for the amount of tissue obtained by the latter method is often inadequate for the pathologist to make a confident histological diagnosis. When the lumps are removed every effort should be made to prevent rupture and spreading the contents.

The quality of frozen sections has improved immeasurably in the last few years and the immediate examination of thyroid specimens can be most helpful but on occasion, owing to the limited number of pieces which can be examined quickly, a final diagnosis from a paraffin section may be required. A useful but less reliable impression of the nature of a nodule may be obtained from the macroscopic examination of the cut specimen. Tumours are generally homogeneous and quite unlike the cystic colloid degeneration of old complicated goitres. In my own series of 44 proven cases of thyroid carcinoma, a correct pre-operative diagnosis was only achieved in two-thirds.

Metastases

As surgeons we have a tendency to think of carcinoma of the thyroid only in terms of swellings in the neck but a small proportion of patients present with signs and symptoms, which are not at first sight due to any primary thyroid disease, in other parts of the body. One of the most intriguing aspects of differentiated thyroid cancer is the unusual manner in which its metastases may behave, appearing on occasion many years after the onset or removal of a primary thyroid tumour or even without any indication as to their origin or remaining unchanged for years.

As every medical student knows, thyroid carcinoma may metastasize to bone but, quite apart from the rarity of the primary disease, in point of fact the number of bony metastases we see is few compared with the great number originating in breast and prostate. During the course of the last twenty-five years, only 6 patients with secondaries in skull or spine from this origin have been treated in the Department of Neurosurgery at the Radcliffe Infirmary and, during more recent years, there were only 2 cases of pathological fractures of other bones due to this cause in our Accident Service.

The histories of some of the cases with neurological signs are not uninteresting, especially in view of the fact that radio-iodine was not then available for their treatment.

One patient – a woman of 63 – came with a large swelling in the skull, which was thought to be probably a meningioma. The whole area of bone was excised and the section showed a well-differentiated carcinoma of the thyroid. The operation was followed by deep X-ray therapy; she remained well for five

years and only then developed a recurrence which responded to further deep X-ray therapy for another three years. Note that this patient survived for eight years after a bony metastasis treated solely by surgery and deep X-ray therapy, the primary tumour never having been removed.

Another patient was perhaps even more remarkable. A thyroid swelling of unknown nature had been removed sixteen years previously from a man then aged 60; ten years later he developed a paraplegia due to spinal metastases, which was treated by decompression and deep X-ray therapy, the section of the tumour showing well-differentiated carcinoma of the thyroid. He survived without symptoms for a further five years before a final fatal paraplegia overtook him.

In 4 out of these 6 cases a thyroidectomy had been performed many years before admission to the neurosurgical unit; in only one of them was the original lesion said to have been malignant but histologically all the secondary tumours showed well-differentiated carcinoma. Only one patient in my own small series came with bony metastases as a presenting symptom: this woman had been referred to the Dermatological Department with a diagnosis of sebaceous cysts of the scalp; their true nature was appreciated and an X-ray showed multiple osteolytic lesions in the skull, which we found were due to follicular carcinoma. Despite a total thyroidectomy and radio-iodine she rapidly developed pulmonary and other distal metastases to which she succumbed.

Pulmonary secondaries may sometimes develop so slowly as to obscure the true nature of the condition, such benign conditions as silicosis being mistakenly diagnosed.

On the other hand we have had our fair share of mistakes and difficulties which have arisen where carcinoma has been suspected or diagnosed wrongly.

Probably the commonest error is to diagnose Hashimoto's autoimmune thyroiditis as carcinoma though, with increasing personal experience and the availability of tests for thyroid antibodies, this should now happen less often than, I regret to say, it still does. Hashimoto's disease can appear at almost any age from 30 to 80; indeed it does not necessarily appear clinically as the bilateral enlargement which, at operation, is always found; nor need the patient show signs of hypothyroidism, a few appear mildly toxic; the thyroid antibodies may not always be present in this disease and indeed may be present in other conditions. Two cases in the early part of our series had a total thyroidectomy carried out on the erroneous assumption that the thyroid was malignant and I think it probable that many other surgeons will admit to having made this mistake. Perhaps this is not so bad as may seem, since carcinoma can be associated with lymphadenoid goitre, though I have not yet encountered such a case. The histology may sometimes be misleading. The biopsy of one patient with a lymphadenoid goitre was originally reported as being a reticulosarcoma and a total thyroidectomy and deep X-ray were advised: further sections, however, were examined and the thyroid antibodies repeated, showing that this was in fact a lymphadenoid goitre: since then this patient has remained well for three years on thyroid extract.

Riedel's thyroiditis may present difficulties, even though the true condition is very much rarer than lymphadenoid goitre. A recent case presented with a very hard goitre and a secondary mass in the chest: a most difficult thyroidectomy, however, showed no tumour, only dense fibrous tissue, but it may well be that a growth has been missed. Calcification in old goitres is common and may cause extreme hardness of the gland; it does not exclude carcinoma which may co-exist with calcification, as I have found on several occasions. Invasion of the thyroid from behind by a post-cricoid carcinoma may simulate thyroid cancer. In a young Siamese girl a very hard lump was found in the lower pole of the thyroid, which was thought to be a malignant nodule but turned out to be a collection of tuberculous lymphatic glands, which were successfully dissected away from the recurrent laryngeal nerve.

Paralysis of the recurrent laryngeal nerves or of the cervical sympathetic is not necessarily pathognomonic of malignancy: on eight occasions I have explored such cases with that in mind but found that the pareses were due to benign conditions, five of which recovered after decompression.

Treatment

Unlike other malignant conditions, where a pre-operative diagnosis is generally accurate, differentiated carcinoma of the thyroid is frequently only recognized after some definitive operation has already been performed; this is undesirable since the management of the patient must very largely depend on the histological nature of the growth; it is, however, one of the difficulties with which we have to contend in this condition. Treatment for the three fairly distinct histology-types of growth is not quite so easy or neat as might appear from books. It is more realistic to describe treatment in the four clinical situations which may be encountered:

(1) A clinically obvious growth about which there is no doubt.
(2) A carcinoma clinically suspected on account of either (*a*) a solitary symptomless swelling, or (*b*) a recent change in a long-standing goitre.

(3) Carcinomas which are entirely unexpected until the diagnosis is made post-operatively by the pathologists.
(4) Carcinomas with distant metastases.

Group 1: Clinically obvious growth: The diagnosis must be confirmed by needle biopsy to determine the exact histology; the majority of these will be found to be anaplastic carcinoma, though squamous cell carcinoma occurs occasionally. The best treatment for all thyroid carcinoma is still surgical excision if it is at all feasible. Unfortunately in anaplastic growths this is rarely possible but operability cannot always be determined until one has tried and such enterprise is occasionally rewarding: the requirements of any surgeon treating cancer are 'a stout heart, a sharp knife and unquenchable optimism' (Gordon-Taylor 1948). Even a palliative operation may be of value in removing a rapidly growing tumour which is distressing and strangling the patient and, combined with a tracheostomy, may give time for deep X-rays. Heroic surgery, however, plays little part in these cases: we have carried out a total laryngectomy and block dissection in one patient, leaving a permanent tracheostomy, which resulted in prolongation of life for a few unhappy months; I would not recommend or repeat this experiment. Deep X-ray, although generally not considered useful in anaplastic carcinoma, has occasionally been valuable, resulting in the survival of an old lady of 80 for two years without recurrence until she died of a cardiovascular accident and also some recovery in another patient, whose brachial plexus was involved in growth and who is alive at two years. We have had no success with radio-iodine in this type of tumour, which corresponds with the experience of Pochin and other experts in this field (Pochin 1956).

Group 2: Clinically suspected carcinoma: The likelihood of malignancy in a solitary node of the thyroid is too well known to require emphasis. The facts that some of these glands turn out to contain multiple nodules at operation which could not be felt previously and that the reported incidence of malignancy varies so widely in no way alter the issue; it is most unprofitable to compare the innumerable statistics which are published on this theme: the possibility is there and cannot be ignored. As Riddell (1954) has emphasized, these lumps should be regarded in exactly the same way as breast lumps – that is to say, they are malignant until proved otherwise. Suspicion is even greater in children, young adults and men at any age, especially if they have been unfortunate enough to have had irradiation of the neck in the past. It is not usually our practice to try to diagnose these tumours pre-operatively by needle biopsy. The nodule should be removed by a generous hemithyroidectomy (which can be carried out with virtually no mortality or morbidity) with a wide margin of normal gland, ligating the main arteries and identifying the nerve and the parathyroid glands if possible. If the nodule is recognized at the time of operation as being malignant, either from frozen section or from gross macroscopical appearances, an examination of the contralateral lobe should be made and, if nodules are present in it, a near total thyroidectomy should be performed, with all adjacent lymph nodes along the carotid sheath and the delphian nodes on the front of and around the trachea being also removed; if the contralateral lobe looks and feels entirely normal it should be conserved.

Group 3: Unsuspected carcinoma: A different situation arises when the malignant nature of the nodule is only revealed post-operatively by an unexpected and disquieting pathological report some days later. Differences of opinion exist as to what, if anything, should be done now for these patients, who are relieved to have had their operations, whose lumps have gone, who with nicely healing wounds are waiting to go home. It is my view that, if an adequate margin of tissue has been removed around the nodule – as it should have been – and if there are no palpable nodules remaining, no further operation is required. However, there are those who, favouring the multicentric origin of carcinoma of the thyroid, hold that a total thyroidectomy should subsequently be performed to remove all the remaining thyroid tissue because of the likelihood of other microscopic areas of malignancy persisting. I do not favour this doctrine myself since the results of the simpler treatment appear to be so good: indeed Crile (1964) has reported that patients who survive five years after removal of a papillary adenocarcinoma without recurrence are extremely unlikely to have any further trouble – that is to say, they are virtually cured. Furthermore, a second operation so soon after the first can have little attraction either for the patient or the surgeon, for the dangers of tetany and injury to the recurrent nerves cannot be discounted and the production of myxœdema is unphysiological, to say the least, in young people: of 12 children undergoing total thyroidectomy at the Mayo Clinic for this condition, no fewer than 11 developed persistent hypoparathyroidism which was described, not unreasonably, as a most distressing complication (Hayles *et al.* 1960).

Finally, in the occasional case in which a recurrence or a new primary does arise all is not lost, for these tumours grow so very slowly that further measures are likely to be successful even

at that stage. I would recommend, therefore, the relatively simple operation of hemithyroidectomy, followed by suppressive treatment with thyroid extract and a regular follow up.

Group 4: Treatment of carcinoma with metastases: The treatment of differentiated carcinoma of the thyroid which has already metastasized to glands, bone or lung presents a situation very different to that usually experienced with other carcinomata. Secondaries may grow so slowly that they may not embarrass or endanger the patient for twenty years or more; the growth may be hormone dependent and in some cases resolve with thyroid medication; finally, under certain circumstances they may assume or be made to take on the normal function of the parent gland. Advantage is taken of these facts in treating the disease.

The papillary type of growth commonly spreads to lymphatic glands so, if the diagnosis is not already obvious from the presence of a tumour in the thyroid gland itself, as for example with a minute, impalpable and occult primary, a biopsy is taken, one of the secondary lymph glands being removed whole. This provides an adequate piece of tissue for histological examination and may prevent fungation through the wound. If the glands are considered operable, a total lobectomy on the affected side is carried out together with a block dissection of the neck – a treatment which has been recognized for many years and yielded good results. Many of the patients are, however, young women in whom the disfigurement of a block dissection cannot entirely be ignored, especially in a disease which is not as lethal as for example secondary glands from carcinoma of the tongue; a modified operation is an alternative, removing the lymph nodes from the posterior triangle and from the length of the carotid sheath but preserving the sternomastoid muscle, the internal jugular vein, the spinal accessory nerve and the cervical plexus. My own experience of this procedure is too small and too recent to know if it will be adequate; I have hopes that it may be so

While there has perhaps been a tendency towards conservatism with regard to block dissection of the neck in papillary cancer, in the United States McClintock *et al.* (1954) have been trying the effect of an extended operation to remove the glands of the anterior mediastinum in continuity by a transsternal approach – thyroid surgeons will be familiar with this technique when exploring for a parathyroid tumour – it would certainly appear to be a logical procedure to clear a wider lymphatic field. Despite the fact that the thyroid drains to lymphatics in front of and around the trachea, these glands are not necessarily the first to be involved; if they were, it is unlikely that block dissection would ever be as successful as it is. It is too early to assess the results of this extended procedure in selected cases.

If the disease recurs in glands or the other lobe of the thyroid some years after the original definite procedures, local excision of the recurrences together with removal of all the remaining thyroid tissue must be performed, followed by deep X-ray therapy and the administration of thyroid extract or, if facilities exist, the use of radio-iodine. We have several patients in this category in whom multiple procedures have been performed and life very much prolonged – in one instance at least for ten years after the first recurrence. Eventually, however, these tumours may take on a more malignant character and terminate rapidly with lung metastases. It is possible that this final development may be delayed by thyroid medication.

When the glands in the neck are frankly inoperable or when distant metastases have spread by the blood stream from a follicular type of carcinoma, it is proper nowadays to attempt treatment by radio-iodine. The object of this is to induce the uptake of a therapeutic dose of radio-iodine in metastases by removal of all normal thyroid tissue, which would normally compete for the iodine, by radical excision which is the quickest and best method of achieving this. If this is impossible on account of local spread or general unfitness for operation, an ablation dose of radio-iodine is used: full myxœdema should develop in two to three months and the secondary deposits may then show a maximum uptake of iodine; when this occurs dramatic improvement may result and pulmonary and other metastases disappear. As a surgeon, I would be rushing in where angels fear to tread if I presumed to comment on these very skilled radiotherapeutic techniques: I can only record that, from our own experience in Oxford and from conversation with other interested surgeons, this desirable result rarely occurs; we have had only 2 cases in this series where such an improvement was achieved. The important point to make is that this type of therapy is likely to give results only with differentiated cancer and that it has generally been ineffective with anaplastic growth. On the other hand, failure of a tumour to take up radio-iodine does not necessarily mean that the method is inapplicable unless all normal thyroid gland has previously been removed. This treatment is too complicated to entrust to departments which are not used to dealing with large amounts of dangerous radio-active material and taking care of the after-effects on bone marrow and lung. It is important, however, to remember that, even if treatment with radio-active iodine is not

successful, local radiotherapy with the administration of thyroxine often effectively prolongs life and controls pain.

The endocrine dependency of some cases of thyroid cancer is one of the most fascinating aspects of this disease and one which is not widely enough known. As long ago as 1937 Dunhill successfully treated two children with recurrent carcinoma of the thyroid with thyroid extract: the tumours disappeared. In 1939 he treated another girl, who had a papilliferous adenocarcinoma, glands and pulmonary metastases: during the ensuing seventeen years while continuing on thyroid all the deposits disappeared and the patient married. His amazing insight into the future took too long to be generally appreciated but it has been amply confirmed (Crile 1957, Thomas 1957). Pituitary suppression with thyroxine or triiodothyronine is now regarded as obligatory for all patients with treated differentiated tumours whether they have metastases or not; the treatment should be continued indefinitely.

Results

The methods of treatment which have been suggested and employed in this series may seem rather conservative and unaggressive. Indeed, compared with some of the more rigorous techniques advised elsewhere, they are so. It is, therefore, incumbent on me to show that my results are at least no worse than those that have been achieved in other series. Although the numbers are small and the follow-up relatively short, I believe that these figures compare reasonably favourably with other series in the United Kingdom (Tables 5 & 6, Figs 5, 6, 7). Surgery and conventional X-ray therapy have been the main methods of treatment. No prophylactic neck dissections have been performed nor any total thyroidectomies for differentiated tumours except when metastases were present. Radio-iodine

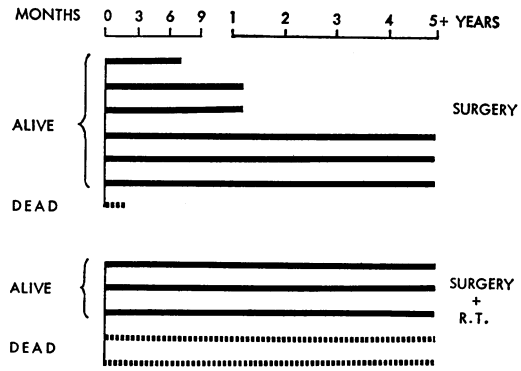

Fig 5 *Treatment of papillary adenocarcinoma*

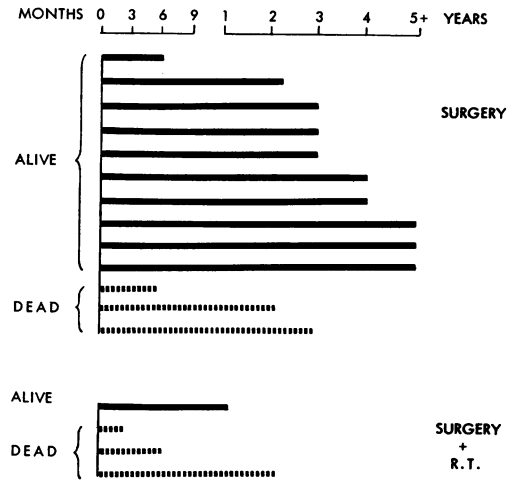

Fig 6 *Treatment of adenocarcinoma*

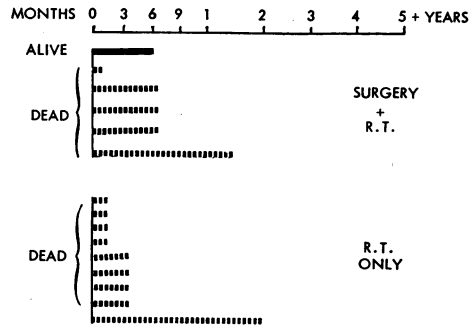

Fig 7 *Treatment of anaplastic carcinoma*

Table 5
Carcinoma of thyroid, 1952–62 inclusive: five-year survivals

	No. of cases	*Alive*	*Dead*	*Percentage survival*
Adenocarcinoma	45	22	23	49
Papillary	11	10	1	90·9
Anaplastic	28	1	27	3·6
Squamous	4	1	3	25
Unclassified	23	6	17	26
Total	111	40	71	

Table 6
Carcinoma of thyroid: author's series

	No. of cases	%	
Adenocarcinoma	17	38·6	65·9
Papillary	12	27·3	
Anaplastic	15	34·1	
Total	44	100	

treatment has been of value in few patients and, although at times dramatic, it would be unrealistic to believe that its use has altered the prognosis very much for the majority of patients suffering from carcinoma of the thyroid. No patient has died as the result of any surgical procedure. The morbidity, however, especially in the undifferentiated group, has been considerable: several patients have had tracheostomies as part of the original operation on the anaplastic growths to relieve dyspnœa and facilitate postoperative irradiation; one patient, aged 60, on whom I operated some fifteen years ago for a papillary growth, sustained a bilateral cord palsy which required a permanent tracheostomy thereafter; she survived, however, for twelve years. Seven patients had pre-operative recurrent nerve palsies due to growth, one of which was relieved by decompression: in 4 patients, however, normal nerves were injured during the course of the thyroidectomy – a small price to pay if a more radical operation was thereby possible. Myxœdema inevitably developed in several patients but surprisingly tetany occurred in only one.

Tables of results do not compare the merits of different methods of treatment so much as the different types of growth encountered.

A good result indicates that the right method was used for that particular growth; bad results occurred when the wrong treatment was chosen or the growth too advanced or intrinsically too malignant. There is an imponderable factor in all treatment of malignancy. In thyroid cancer the papillary tumours do well and the anaplastic ones badly – in this series the latter disastrously so, hardly better I would surmise than those treated by Sir James Berry and his contemporaries. This is, however, the general pattern of this type of the disease. It would be complacent in the extreme to accept the results as they are: it should be, I believe, within our power with the existing methods to improve the treatment of the intermediate group of adenocarcinomata, which at the moment has a 49% five-year survival; more radical surgery and more efficient use of radioiodine may save the marginal cases. I doubt if any existing method will improve the results in the undifferentiated anaplastic group. This must come through some other development such as chemotherapy, which has already been tried with some success.

Acknowledgments: I am grateful to my colleagues in the United Oxford Hospitals and the Oxford Region for the information which they have so kindly given me about their cases; to Miss C Hunt, Records Officer of the Oxford Regional Hospital Board; to Miss M C McClarty, Medical Artist and Mr E L P Tugwell of the Photographic Department of the United Oxford Hospitals, for their enthusiastic help.

REFERENCES

Berry J (1901) Diseases of the Thyroid Gland and their Surgical Treatment. London
Billroth T (1878) Surgical Pathology and Therapeutics. New Sydenham Soc., London; **76**, 442
Bland-Sutton J (1901) Tumours Innocent and Malignant. 2nd ed. London; p 283
Crile G jr
(1957) *Cancer* **10**, 1119
(1964) *Ann. Surg.* **160**, 178
Doniach I (1956) *Proc. R. Soc. Med.* **49**, 173
Dunhill T (1937) *Trans. med. Soc. Lond.* **60**, 234
Gordon-Taylor G (1948) *Proc. R. Soc. Med.* **41**, 119
Hayles A B, Kennedy R L J, Beahrs O H & Woolner L B (1960) *J. Amer. med. Ass.* **163**, 21
Heister L (1748) General System of Surgery. 3rd ed. London
Inglis J (1838) Treatise on English Bronchocele. London
King T W & Cooper A (1836) *Guy's Hosp. Rep.* **1**, 429
McClintock J C, Stranahan A & Alley R D
(1954) *Amer. Surg.* **20**, 726
Pochin E E (1956) *Proc. R. Soc. Med.* **49**, 177
Riddell V (1954) Progress in Clinical Surgery. Ed. R. Smith London; chap 23, p 265
Thomas C G (1957) *Ann. Surg.* **146**, 879